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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/884,889	06/19/2001	Dan E. Robertson	DIVER1100-4	1715

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EXAMINER	
PROUTY, REBECCA E	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 07/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/884,889	ROBERTSON ET AL.	
	Examiner	Art Unit	
	Rebecca E. Prouty	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-55,93,94 and 98-119* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-55,93,94 and 98-119* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 1-41, 55-92 and 95-97 have been canceled. Claims 42-54, 93, 94, 98-117 and newly presented claims 118 and 119 are still at issue and are present for examination.

Applicants' arguments filed on 4/22/04, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claims 42-54, 93, and 98-119 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is explained in the previous Office Action.

Applicants argue that the claims have been amended to be directed to methods for generating variants comprising providing a genus of catalase-encoding nucleic acids. However it is noted that claim 42, part (c) is not so limited as to require that the sequence encode a catalase. As such contrary to applicants arguments none of Claims 42-54 and 98-119 are limited to methods which include providing a genus of catalase-

encoding nucleic acid. Furthermore, while claim 93 has been amended to be directed to methods for generating variants comprising providing a genus of catalase-encoding nucleic acids, the only structural limitation on the genus of catalase-encoding nucleic acids is that it comprise 30 consecutive nucleotides of a sequence having 65% identity to SEQ ID NO:7 or 35 consecutive nucleotides of a sequence having 65% identity to SEQ ID NO:5. As stated by applicants the requirements for written description of a genus of nucleic acids as set forth in University of California v. Eli Lilly & Co., 43 USPQ2d 1398 (Fed. Cir. 1997) may be achieved by a recitation of a representative number of DNAs defined by nucleotide sequence or a recitation of structural features common to members of the genus, which features **constitute a substantial portion of the genus**. Claim 93 recites use of nucleic acids which comprise only 30 consecutive nucleotides of a sequence having 65% identity to SEQ ID NO:7 or 35 consecutive nucleotides of a sequence having 65% identity to SEQ ID NO:5 as the only recited structural limitation of the claim. These recited structural features of the genus do not constitute a substantial potion of the genus as the remainder of the structure of a nucleic acid encoding a polypeptide with catalase is completely undefined. Fragments

consisting of only 30 consecutive nucleotides of a sequence having 65% identity to SEQ ID NO:7 or 35 consecutive nucleotides of a sequence having 65% identity to SEQ ID NO:5 are highly unlikely to have esterase activity, constitute only a very small portion of the structure of the only disclosed species (SEQ ID NO:5 and 7) and the specification does not define the remaining structural features necessary for members of the genus to be selected. As such these structural features are insufficient to be representative of the structural features of all members of the genus.

Claims 42-54, 93, and 98-119 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of generating a variant catalase comprising creating a library of variants of SEQ ID NO:5 or 7 by modifying (i.e., adding, deleting or substituting) one or more nucleotides of SEQ ID NOS:5 or 7, expressing said modified sequences, screening the proteins produced from said modified sequences for catalase activity and selecting a variant sequence which encodes a protein having catalase activity, does not reasonably provide enablement for methods of generating variants of SEQ ID NO:5 or 7 or variants thereof as claimed. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to use the invention commensurate in scope with these claims. The rejection is explained in the previous Office Action.

Applicants argue that the specification enabled the invention as claimed. Applicants refer to declarations by inventor Jay Short, who declares that the state of the art at the time of the invention and the level of skill of the person of ordinary skill in the art was very high. Dr Short's declarations further states that one of skill in the art at the time of the invention could use the teachings of the specification and other protocols known in the art to screen for nucleic acids encoding polypeptides having catalase activity and that while the number of samples needed to be screened may have been high, the screening procedures were routine and successful results predictable. According to Dr. Short's declaration, knowledge of the specific structural elements which correlate with catalase activity would not have been required to create variants and test them for activity. Applicants further argue that enablement is not precluded by the necessity to screen large number of compositions as long as that screening is routine. Applicants refer to *Hybritech, Inc. v. Monoclonal Antibodies, Inc.* as support for the argument that the claimed

invention is enabled even if there is a need to screen large numbers of negatives to find a sample with the desired activity.

As indicated in the previous Office Action, the specification is completely silent in regard to which are the amino acid residues which can be substituted, deleted, or inserted in the nucleic acids of SEQ ID NO:5 or 7 to obtain structural homologs of the nucleic acid of SEQ ID NO:5 or 7 as recited in the claims which encode proteins with catalase activity. In addition, the specification does not provide any clue as to which 30 consecutive base fragments of the nucleic acid of SEQ ID NO:7 or 35 consecutive base fragments of the nucleic acid of SEQ ID NO:5 are required to encode proteins with catalase activity nor does it provide any clue as to which fragments of a nucleic acid having at least 65% sequence identity to the SEQ ID NO:5 or 7 and encoding an catalase are essential for catalase activity. The prior art clearly teaches the unpredictability of assigning function based on structural homology and how small structural changes can lead to major changes in function. For specific teachings of such unpredictability, see Bork, Broun et al., Van de Loo et al., Witkowski et al. and Seffernick et al. Each of these references which are presented merely as evidence of the state of the art

as previously characterized by the examiner, shows that even small changes in the primary structure of an encoded protein can have substantial effects on function. Furthermore, it should be noted that applicants claims encompass the use of not only nucleic acids having minor changes in structure from SEQ ID NO:5 or 7, but include nucleic acids with major changes as well. Therefore, in the absence of any information as to how structure correlates with function, one of skill in the art would have to go through the burden of undue experimentation to isolate/make the nucleic acids as encompassed by the claims, to practice the full scope of the claimed invention.

Applicants current claims appear to have two fundamental problems with regard to the scope of enablement. The first is with regard to a skilled artisan's ability to **make** all nucleic acids which will be used within the claimed methods. The declarations of Dr Short state that methods of making variants of a known sequence are well known in the art, including methods which result in more than one change in a sequence and that the skilled artisan is capable of screening any specific sequence to determine if it has activity. This is not disputed by the examiner. However, applicants arguments amount to a conclusion that screening for a needle in a haystack should be enabled

because the artisan knows how to look for it, can identify it when it is seen and knows it is there somewhere. This is not case. It is well established that while enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the **specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.** The only guidance present in the specification for selecting the needle in the haystack (i.e., a nucleic acid comprising 30 consecutive base fragments of the nucleic acid of SEQ ID NO:7 or 35 consecutive base fragments of the nucleic acid of SEQ ID NO:5 or having 65% identity of SEQ ID NOS: 5 or 7 and having catalase activity) is the sequences of SEQ ID NOS:5 and 7 themselves. This is clearly insufficient given that the claims require little structural homology to these sequences to be maintained (i.e., the haystack is enormous) and the known fact that only a very minuscule portion of the sequences having claimed structural features will have catalase activity (i.e., the needle is very tiny).

The second fundamental problems with regard to the scope of enablement of the instant claims is with regard to a skilled artisan's ability to **use** all nucleic acids which will be produced by the claimed methods. The claimed methods do not

include a step of screening the variants made for those which have catalase activity nor to they limit the number of changes in the sequence of the original nucleic acid that are made in any way. Thus in reality the product of the instant methods is **any** nucleic acid under the sun. The skilled artisan clearly does know how to use this scope of nucleic acids and the specification teaches only the use of the products of the methods as catalases. However, not all nucleic acids encode catalases. While the skilled artisan is capable of screening any variant sequence produced for those which do encode such an enzyme, this is the only means taught by the specification for selecting those variants having the utility discussed in the specification, and the claims **are not** limited to methods encompassing such a step. How does the skilled artisan use the products of the remaining methods within the scope of the instant claims? Dr Short's declarations do not address this question at all.

Claim 94 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of generating a variant catalase comprising creating a library of variants of SEQ ID NO:5 or 7 by modifying (i.e., adding, deleting or substituting) one or more nucleotides of SEQ ID

NOS:5 or 7, expressing said modified sequences, screening the proteins produced from said modified sequences for catalase activity and selecting a variant sequence which encodes a protein having catalase activity, does not reasonably provide enablement for methods of generating a variant catalase comprising modifying (i.e., adding, deleting or substituting) one or more nucleotides of SEQ ID NOS:5 or 7. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants did not specifically address the instant rejection, instead traversing the rejection of Claims 42-54, 93, and 98-119 all together. The instant claim was separated out from the other in the previous Office Action because its deficiencies in enablement are limited only to a skilled artisan's ability to **use** all nucleic acids which will be produced by the claimed methods. As stated above, The claimed methods do not include a step of screening the variants made for those which have catalase activity nor to they limit the number of changes in the sequence of the original nucleic acid that are made in any way. Thus in reality the product of the instant methods is **any** nucleic acid under the sun. The skilled artisan

clearly does know how to use this scope of nucleic acids and the specification teaches only the use of the products of the methods as catalases. However, not all nucleic acids encode catalases. While the skilled artisan is capable of screening any variant sequence produced for those which do encode such an enzyme, this is the only means taught by the specification for selecting those variants having the utility discussed in the specification, and the claims **are not** limited to methods encompassing such a step. How does the skilled artisan use the products of the remaining methods within the scope of the instant claims? Dr Short's declarations do not address this question at all.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 43, 50, and 93 are rejected under 35 U.S.C. 102(b) as being anticipated by Trakulnaleamsai et al. as evidenced by Loprasert et al. (reference AC of applicant's PTO-1449). The rejection is explained in the previous Office Action.

Applicants argue that Trakulnaleamsai et al. do not teach methods of mutating a nucleic acid having at least 65% identity to SEQ ID NO:5 or 7 or at least 65% identity to SEQ ID NO:5. This is not persuasive because claim 93 recites the use of any nucleic acid comprising a fragment of at least 35 consecutive nucleotides of a sequence having about 65% identity to SEQ ID NO:5. The nucleic acid of Trakulnaleamsai et al. comprises at least a regions of 35 nucleotides each having 86% identity to the corresponding portion of SEQ ID NO:5 (i.e., nucleotides 513-549 of Trakulnaleamsai et al are 86% identical to residues 459-498of SEQ ID NO:5 respectively).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35

U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 43-53, 93 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trakulnaleamsai et al. in view of Short (US Patent 5,939,250). The rejection is explained in the previous Office Action.

Applicant has not presented any arguments specifically traversing this rejection but instead relies upon the traversal discussed above. Therefore, this rejection is maintained for the reasons presented above.

Claims 42, 43, 54, and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trakulnaleamsai et al. in view of Short (US Patent 6,479,258). The rejection is explained in the previous Office Action.

Applicant has not presented any arguments specifically traversing this rejection but instead relies upon the traversal discussed above. Therefore, this rejection is maintained for the reasons presented above.

Claims 42-53, and 93-117 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trakulnaleamsai et al. in view of Short (US Patent 5,939,250) and Robertson et al. (WO

98/00526). The rejection is explained in the previous Office Action.

Claims 42, 43, 54, 55 and 93-119 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trakulnaleamsai et al. in view of Short (US Patent 6,479,258) and Robertson et al. (WO 98/00526). The rejection is explained in the previous Office Action.

Applicants argue that the parent applications (08/951,844 and 08/674,887 provide support for the current claims and thus Robertson et al. is not proper prior art. This is not persuasive because each of the instant claims includes limitations which are not supported by the parent applications. The parent applications do not However, the disclosure of the parent applications fails to disclose methods of mutagenesis of the disclosed catalase genes. The passages cited by applicants from the parent application are defining the scope of the nucleic acids claimed (i.e., state that variants of SEQ ID NOS:5 and 7 are part of the nucleic acids of the invention) They do not state that the invention is methods of mutagenesis of the disclosed catalase genes. As such Robertson et al. is prior art to the instant claims. It should be noted that many other limitations of many of the instant claims also lack support in

the parent applications. For example the recitation of nucleic acids having 65% identity to SEQ ID NOS:5 or 7 or nucleic acids comprising 35 consecutive nucleotides of SEQ ID NO:5 are not present in the parent application.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (571) 272-0937. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura

Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Rebecca Prouty
Primary Examiner
Art Unit 1652